REMARKS/ARGUMENTS

Support for the Amendments

Applicants have amended the first sentence of the specification to establish priority so as to be consistent with the filing receipt for the present application mailed by the United States Patent and Trademark Office on May 24, 2004.

Applicants have amended Claim 5 to be in proper form for a use claim, as suggested by the Examiner.

These amendments are being presented in order to correct the formalities previously identified and to place the application in better condition for appeal. No new matter or substantive issues are presented with these amendments.

Priority

Applicants thank the Examiner for pointing out the inadvertent omission of the priority reference. Applicants have proposed the amendment identified above to correct his formality.

Withdrawn Rejections

Applicants thank the Examiner for considering Applicants argument filed on October 3, 2008 and withdrawing the rejection of Claims 1-5 under 35 USC 112.

The 101 Rejections

The Examiner rejected Claim 5 under 35 USC 101 as a use claim that did not recite any steps. Applicants have amended Claim 5 to correct this formality.

The 103 Rejections

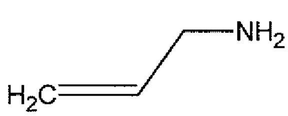
The Examiner has rejected Claims 105 as being unpatentable under 35 USC 103 over US 3,320,317 ("Rogers") in view of WO/95/05184 ("WO '184"). Applicants respectfully traverse the rejection and present the following clarifying remarks:

As the Examiner has stated, the present claims are directed to a method for decreasing absorption of phosphate or oxalate from the gastrointestinal tract which comprises the step of administering an effective amount of a formulation comprising a water soluble polyether glycol polymer. The Examiner has considered the arguments previously presented by Applicants but in large part has found them unconvincing. Therefore, Applicants will try to present the arguments from a different point of view, focusing on the following: 1) The chemistry of the present application contrasted with the chemistry of Rogers; 2) The chemistry of Rogers contrasted with the chemistry of WO '184; 3) The motivation to combine Rogers and WO '184 based on chemistry; 4) The difference between the chemistry of Rogers and WO '184 and the present invention; 5) The difference between the mechanism of Rogers and WO '184 and the present invention; and 6) The motivation to combine Rogers and WO '184 based on the mechanism.

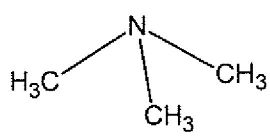
1) The chemistry of the present application contrasted with the chemistry of Rogers

The Examiner states that Rogers teaches quaternary ammonium adduct of polyepichlorohydrin. Applicants would like to point out that the polymers taught by Rogers are different than those [claimed] in the present application.

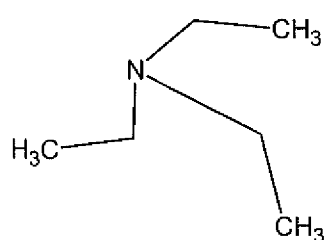
First of all, the Examiner has stated that Rogers makes his polymers from epichlorohydrin and allylamine; however, Applicants would like to point out that this is incorrect as Rogers never mentions allylamine (which is a specific vinyl compound represented as H2C=CH-CH2NH2) but instead talks about tertiary alkyl amines in general – giving specific examples of trimethylamine and triethylamine. These are very different from the allylamine, which is a primary amine rather than a tertiary amine.



Allylamine

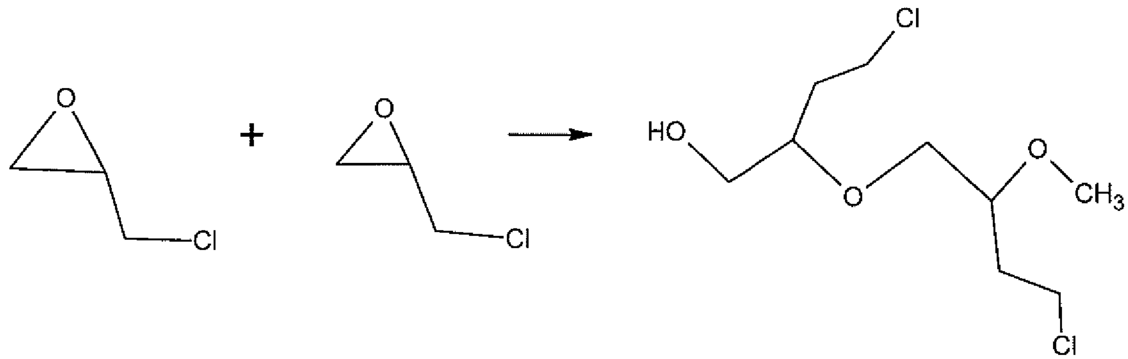


trimethylamine

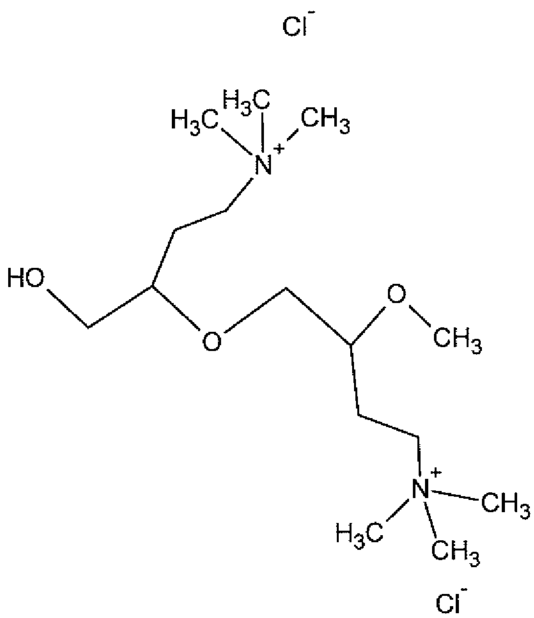


triethylamine

Missing this difference in amines leads to a misunderstanding of the chemistry of the reactions, and Applicants wish to address this more deeply. For Rogers, an acid catalyzed ring opening of epichlorohydrin is performed to create polyepichlorohydrin:



(Applicants intend for this to represent just a short section of the polymer and this is not intended to say one end ends with an OH and the other end ends with a CH3 – that is just the drawing program.) Rogers then reacts this polyepichlorohydrin with a tertiary amine. So, for the trimethylamine reaction, the result is:



This is a polymer with oxygens in the backbone and quaternary nitrogens projecting from the backbone. The oxygens in the backbone make it water soluble (mentioned in the present application Summary of Invention as "water-soluble polyether glycol polymer").

2) The chemistry of Rogers contrasted with the chemistry of WO '184

The Examiner goes on to state that the polymers of Rogers are made from epichlorohydrin and allylamine and that the polymers of WO '184 are also made from monomers of epichlorohydrin and allylamine, and indicates that this would lead one of ordinary skill in the art to combine the two references.

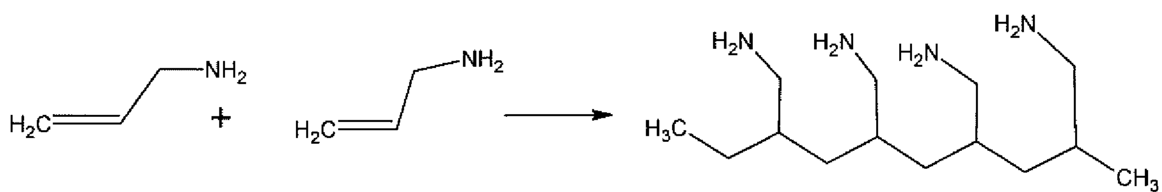
Applicants agree that Rogers does not teach decreasing the absorption of phosphate or oxalate from the gastrointestinal tract. However, Applicants traverse the Examiner's statement that this deficiency is cured by WO '184. The polymers taught

by Rogers and WO '184 are very different polymers, and therefore there would be no motivation for one skilled in the art to look to combine the two references.

Applicants will describe just how different the polymers taught by Rogers and WO '184 are by describing the chemistry behind the two references:

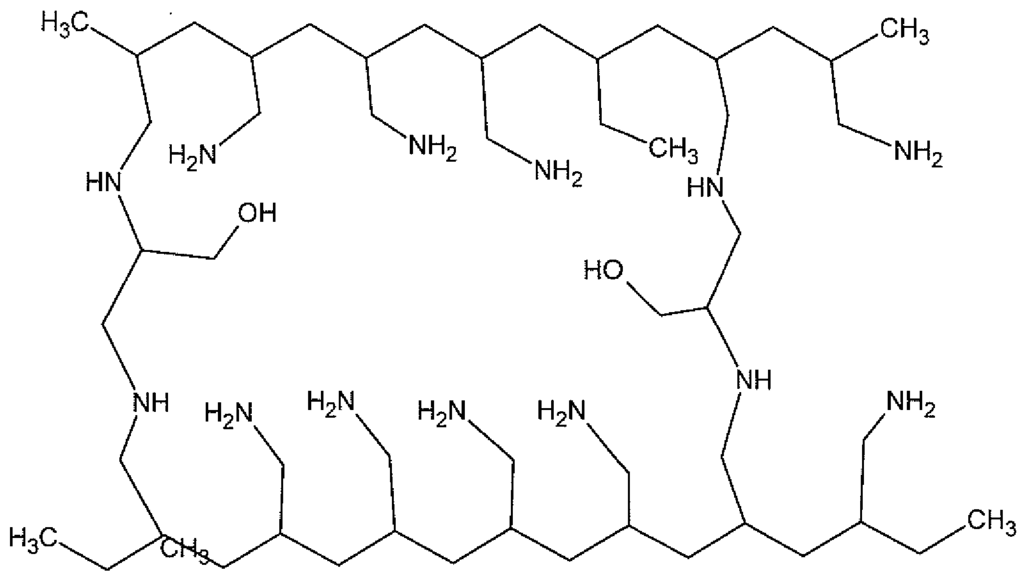
The chemistry of Rogers is as described above. In contrast to the chemistry of Rogers which uses epichlorohydrin and a tertiary amine as monomers, WO'184 starts by polymerizing allylamine into polyallylamine. Although the Examiner states that WO'184 teaches using epichlorohydrin and allylamine as the monomers in their polymer, that is incorrect. Rather, in the summary of the invention, first paragraph, WO'184 makes it clear that the use of epichlorohydrin is only optional and as a crosslinker, not a monomer, stating "Examples of preferred crosslinking agents include epichlorohydrin, 1,4 butanedioldiglycidyl ether, 1,2 ethanedioldiglycidyl ether,".... So WO '184 teaches making a different compound, not the same compounds as Rogers, contrary to what the Examiner has stated.

Applicants further describe this by drawing the reaction taught in WO'184, which is:



Allylamine polyallylamine

WO'184 then crosslinks this polyallylamine with various agents. One of those agents is epichlorohydrin, as the patent examiner states, but this is now a based-catalyzed ring opening of epichlorohydrin which opens differently and does not leave the oxygen in the chain. Instead, it produces:



This molecule obviously has many more primary amines than the Rogers polymer and has no quaternary amines. The WO'184 polymer is not soluble in water. Thus, just because both polymers used epichlorohydrin and an amine, they do not give equivalent polymers. This can be seen from the patents and is not just evident in applicants arguments, as Figure 1 in WO'184 shows a backbone of carbon-carbon bonds with no oxygens, while Rogers specifically shows in Column 1 a polymer with two carbons and an oxygen in the backbone and repeats this in Claim 1.

Therefore, as shown here, the polymers in Rogers and WO '184 are very different – one is not soluble in water with many primary amines, and the other that is soluble in water with many quaternary amines.

3) The motivation to combine Rogers and WO '184 based on chemistry

The Examiner states that Rogers does not teach that quaternary ammonium adduct of polyepichlorohydrin can be utilized to decrease the absorption of phosphate or oxalate from the gastrointestinal tract but that this deficiency is cured by WO '184. Applicants traverse this argument for the following reasons.

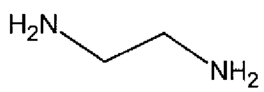
As described above, the polymers in Rogers and WO '184 are very different (one not soluble in water and with many primary amines versus one that is water soluble and having many quaternary amines). Therefore, one of ordinary skill in the art would <u>not</u> be motivated to combine these references. Nothing in either of the references would cause one to look at the other references when neither the polymers nor the intended use for the polymers are relevant to those taught by the other reference. WO '184 does not cure the fact that Rogers does not teach the utilization of the polymers described therein to decrease the absorption of phosphate and oxalate from the gastrointestinal tract.

The Examiner futher states that WO'184 teaches oral administration of a phosphate-binding polymer with a quaternary amine and that one of ordinary skill would obviously have used the polymer of Rogers to do the same binding as seen in WO'184.

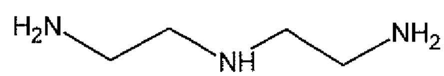
4) The difference between the chemistry of Rogers and WO '184 and the present invention

The polymers described in the present application are not the same as those described in Rogers nor in WO '184, contrary to what the Examiner has stated.

Applicants would like to point out that the polymers in the present application include amines that are not from either of these classes of amines (neither allylamine of WO'184 nor tertiary amines of Rogers). Our Example 3 derivatizes the polyepichlorohyrin base polymer of Rogers with diethylenetriamine (DETA) – which is neither a tertiary amine nor allylamine. Our Example 4 derivatizes the base polyepichlorohydrin with ethylenediamine (EDA), again neither a tertiary amine nor allylamine.



EDA



DETA

So, these examples of our polymers are not like either of the two patents.

5) The difference between the mechanism of Rogers and WO '184 and the present invention

The Examiner states (same paragraph, page 9) that the method of removing phosphate or oxalate is achieved via ion exchange. Applicants respectfully point out that ion exchange is merely having a positively charged ion which is initially ionically bound to one negatively charged ion "exchange" that negatively charged ion for a different one. By contrast, the present application specifically talks about chelation (also using the word complexation) rather than just ionic bonding in the background section. Chelation (or complexation) does involve ionic interactions between oppositely charged moieties, but require more than one moiety of one of the charges to hold or encase or enclose the moiety of the other charge. So, a phosphate has several negative charges (from -1 to -3 depending on pH) "spread out" over the entire polyatomic anion. Thus, to chelate (or complex) with it, two or more amines would be required to surround it by interacting with negative charge on different parts of the polyatomic anion. This is very different than just ion exchange because ion exchange does not depend on the amines being at specific distances to be able to reach around the negative moiety – ion exchange just depends on charges. For this reason, Claim 1 is drafted to state that the polymer is constructed in such a way that it "permits complexation with phosphate or oxalate." Even WO'184 shows that they are not just

having ion exchange in their first table in the Examples section (page 10) where they show a 30 fold difference in phosphate binding within the table and a 10 fold difference in such similar compounds as the first and fourth ones in the table.

These differences in polymer and the 30 fold difference in phosphate binding with different polymers in WO'184 would not give anyone of ordinary skill in the art any "reasonable expectation that the polymers of Rogers would additionally be suitable for binding phosphate." It might be of interest to someone skilled in the art of making flocculants and skilled in the very different art of treating phosphate removal from animals with phosphate overload to try it, but those are two very different fields of art so that it would be very unlikely to see both of them or to connect them as saying that two very different polymers (one not soluble in water and with many primary amines versus one that is water soluble and having many quaternary amines) might be useful for the same thing.

Applicants would like to point out that the differences identified here, both in the chemistry and in the mechanism of binding, are present in the patents, not just in the statements the Applicants are making.

6) The motivation to combine Rogers and WO '184 based on the mechanism

At the bottom of page 9, the Examiner states that because the polymers of WO'184 and Rogers are made from the same monomers, we cannot say that Rogers' polymers would not be suitable for administration to animals and that we have provided no evidence that they cannot be administered to animals. Applicants first note that, as discussed above, the polymers of WO '184 and Rogers are different and therefore one of ordinary skill in the art would not be motivated to combine the references based on chemistry. Applicants further point out that it would not be obvious to take a compound that is designed for flocculation of sewage (as with the polymer of Rogers) and expect it to be tolerated in oral administration to animals.

The Wikipedia definition of flocculant is:

"**Flocculants**, or **flocculating agents**, are chemicals that promote **flocculation** by causing colloids and other suspended particles in liquids to aggregate, forming a floc. Flocculants are used in water treatment processes to improve the sedimentation or filterability of small particles. For example, a flocculant may be used in swimming pool or drinking water filtration to aid removal of microscopic particles which would otherwise cause the water to be turbid (cloudy) and which would be difficult or impossible to remove by filtration alone.

Many flocculants are multivalent cations such as aluminium, iron, calcium or magnesium. These positively charged molecules interact with negatively charged particles and molecules to reduce the barriers to aggregation. In addition, many of these chemicals, under appropriate pH and other conditions such as temperature and salinity, react with water to form insoluble hydroxides which, upon precipitating, link together to form long chains or meshes, physically trapping small particles into the larger floc."

This definition would not motivate one skilled in the art to use the polymers of Rogers in the application described in WO '184, as the phosphates and oxalates are

dissolved in water rather than being particles suspended in water. But one would not consider flocculants to be safe in oral administration as one would expect a flocculant to precipitate a wide variety of ions which would be expected to cause damage to the animal.

For all of these reasons, Applicants believe that the present invention is not obvious over Rogers in view of WO '184 under 35 USC 103.

Conclusion

Applicants respectfully request reconsideration of the application in view of the foregoing amendments and remarks. Alternatively, Applicants respectfully request entry of the amendments above and believe that the application now stands in better condition for appeal.

Respectfully submitted,

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